REMARKS

Claims 9-12, 14 and 15 presently appear in this case. No claims have been allowed. The official action of February 23, 2004, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

It is noted with appreciation that all of the previous rejections of record have now been withdrawn.

Claims 9-11 and 13-15 have been rejected under 35 U.S.C. §112, first paragraph, because, while being enabling for a method of treating a demyelinating disease of the CNS or PNS, the specification does not reasonably provide enablement for a method of treating all possible neurological diseases or disorders by administering an effective amount of IL6RIL6 chimera. This rejection is respectfully traversed.

The examiner concedes that the present invention is enabling for a method of treating a demyelinating disease of the CNS or PNS, and it is noted that claim 12 has not been made subject to this rejection. However, the present specification is also enabling for the protection of neurons from pathological insults, for example, excitotoxicity (cell death caused by excessive activation of glutamate receptors). The examiner's attention is invited to Examples 9 and 10 of the present specification, showing that the IL6RIL6 chimera provide protection from NMDA-induced hippocampal cell death,

and from glutamate induced neurotoxicity, and from toxicity caused by the withdrawal of NGF. In this regard, reference is made to the present specification at page 5, lines 18-25, page 7, lines 13-18, and page 10, lines 17-24. It should be noted that Example 9 actually describes a model for Parkinson's disease. See Gerlach et al, "New Horizons in Molecular Mechanisms Underlying Parkinson's Disease and in Our Understanding of the Neuroprotective Effects of Selegaline," *J Neural Transm Suppl* 48: 7-21 (1996), the abstract of which is attached hereto.

The present claims have now been amended to specify that the method is either for inducing myelination or remyelination of neurons as the examiner admits is supported by an enabling disclosure, and also for protecting neurons from pathological insults. As the claims are now all limited to specific applications that are supported by the specification and no longer read on the treatment of all possible neurological diseases or disorders, reconsideration and withdrawal of this rejection is in order.

Claims 9-15 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The examiner states that claims 9 and 10 omit essential steps in not reciting a results step. Further, the examiner states that the acronym

"IL6RIL6" should be recited by its full name in the first independent claim.

Claim 9 has now been amended to specify that the administration step results in the induction of myelination or remyelination of neurons or the protection of neurons from pathological insults, thus obviating the first part of this rejection. Furthermore, the full name of the chimera has been inserted in claim 9. Claim 10 has now been made to be dependent from claim 9. Accordingly, it is submitted that this rejection has now been obviated. Reconsideration and withdrawal thereof is therefore respectfully urged.

Claims 9-15 have been rejected under 35 U.S.C. §102(b) as being anticipated by Revel. The examiner states that Revel discloses a pharmaceutical composition comprising an IL6RIL6 chimera, and a method of using such chimera in a the preparation of a medicament for treating neurological diseases, citing pages 7-8, and page 11, lines 21-28. Thus, the examiner concludes that this disclosure meets all of the limitations recited in claims 9-15. This rejection is respectfully traversed.

The Revel reference discloses IL6RIL6 chimera and their use for various indications, including the treatment of the liver, for treating cancer, for enhancing bone marrow transplantation, and other conditions such as neurological

disorders in general. The present claims are not directed to the treatment of neurological disorders in general, but are very specific to the induction of myelination and remyelination of neurons, and to the protection of neurons from pathological insults. That the chimera of Revel would be useful for these specific indications would not have been anticipated or made obvious by the general disclosure of treating "neurological disorders". The results of the examples in the present specification would have been surprising to anyone of ordinary skill in the art reading Revel. Certainly, Revel does not anticipate the treatment of multiple sclerosis, as provided in claim 12. While multiple sclerosis is a neurological disorder, a general reference to the treatment of neurological disorders does not anticipate the specific treatment of MS. As stated at MPEP 2131.01, to anticipate a claim, the reference must teach every element of the claim. As the Revel PCT publication does not teach the elements of inducing myelination or remyelination of neurons, or the element of protecting neurons from pathological insults, it cannot be considered to be in anticipation of any of the present claims. Reconsideration and withdrawal of this rejection is therefore also respectfully urged.

It is submitted that all of the claims now present in the case clearly define over the references of record and

fully comply with 35 U.S.C. §112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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1: J Neural Transm Suppl. 1996;48:7-21. Related Articles, Links

New horizons in molecular mechanisms underlying Parkinson's disease and in our understanding of the neuroprotective effects of selegiline.

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There have been many claims that the selective monoamine oxidase type B (MAO-B) inhibitor selegiline may have distinct properties in slowing the progression of Parkinson's disease (PD). Degeneration of nigro-striatal dopaminergic neurons is the primary histopathological feature of PD. Although many different hypotheses have been advanced, the cause of chronic nigral cell death and the underlying mechanisms remain elusive as yet. Therefore, there is no clear knowledge regarding an understanding of the reported effects of selegiline on the progression of PD. However, there is a considerable body of indirect evidence that oxidative stress may play a role in the pathogenesis of this illness. Oxidative stress refers to cytotoxic consequences of hydrogen peroxide and oxygen-derived free radicals such as the hydroxyl radical (.OH), the superoxide anion (.O2), and nitric oxide (NO), which are generated as byproducts of normal and aberrant metabolic processes that utilize molecular oxygen. On the other hand, an increasing body of experimental data has implicated excitotoxicity as a mechanism of cell death in both acute and chronic neurological disease. One of the receptor which is particularly involved in the toxic effects of excitatory amino acids is the NMDA (N-methyl-D-aspartate) receptor. Excessive stimulation of this type of receptor by glutamic acid or NMDA agonists leads to a massive influx of calcium ions into the neuron followed by activation of a variety of calcium-dependent enzymes, impaired mitochondrial function, and the generation of free radicals. This article will consider the concept that excitotoxicity is linked with the generation of free radicals. In view of this idea it will be further discussed how selegiline might exert its neuroprotective effects via indirect actions on the polyamine binding site of the NMDA receptor. Under treatment with the MAO-B inhibitor selegiline, the degradation of putrescine via MAO, a key factor in regulating the polyamine metabolism, might be diminished in the Parkinsonian brain, which in turn would suppress the polyamine synthesis. Hence, the reported neuroprotective effect of selegiline might also receive a contribution from the diminished potentiation of the NMDA receptor by the polyamine binding site. On the other hand, since N1-acetylated spermine and spermidine are also good substrates of MAO-B, it is likely that these compounds will be present in the brain in increased concentrations. It therefore seems possible that they will exert a neuroprotective effect via an antagonistic modulation of the polyamine binding site of the NMDA receptor.

Publication Types: